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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,054	06/07/2006	Youe-Kong Shue	8031-011-US	7988
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EXAMINER KRISHNAN, GANAPATHY				
ART UNIT 1623		PAPER NUMBER		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/574,054

Applicant(s)

SHUE ET AL.

Examiner

Ganapathy Krishnan

Art Unit

1623

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 March 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11, 16-18 and 23-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11, 16-18 and 23-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-06)
Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

The amendment filed 3/24/2010 has been received, entered and carefully considered.

The following information has been made of record in the instant amendment:

1. Claims 12-15, 19-22 and 31-33 have been canceled.
2. Claims 1, 8-9 and 18 have been amended.
3. Remarks drawn to rejections under 35 USC 102 and 103.

The following have been overcome:

4. The rejection of claims 12-15 and 19-22 has been rendered moot by cancellation of the said claims.
5. The rejection of Claims 18, 23-24 and 27-28 under 35 U.S.C. 102(b) as being anticipated by Henderson (US 5,587,363, of record) has been overcome by amendment to claim 18, which now recites a method of treating synovitis or subchondral bone edema. Henderson et al do not teach the treatment of synovitis or subchondral bone edema using the aminosugars glucosamine or N-acetyl glucosamine or galactosamine or their salts.

Claims 1-11, 16-18 and 23-30 are pending in the case.

The following rejections are made of record necessitated by amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-11, 16-18 and 23-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weidner (WO 03/002117, of record) in view of Petrus et al (US 6,656,925, of record) and Speck (US 4,870,061, of record).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Weidner, drawn to aminosugar comprising compositions, teach the treatment of synovitis via administration of the said composition comprising effective amounts of the aminosugar(s) to individuals suffering from osteoarthritis/degenerative arthritis (page 2, lines 15-31; page 20, lines 19-25; page 19, line 41 through, page 20, line 3 ; limitations of claims 1, 9 and 18). Suitable aminosugars for use are glucosamine, galactosamine, their salts and derivatives including N-

acetyl derivatives and hydrochloride salts (page 10, lines 30-35, limitations of claims 1-2, 9-11, 27, 28-for specific aminosugars). The compositions can be administered as a polymer implant or as an intramuscular injection (page 15, lines 1-10; part of limitations of claims 3-4, 6, 8 and part of claim 10 and 29). The formulations can be in the form of suspensions and gels (page 15, lines 36-39; limitations of claims 3-5, 7, 8 and part of claim 29). Gel-forming agents and gel bases can also be used (page 17, lines 9-15; this is also seen to teach the limitations of claim 7).

However, Weidner does not specifically teach treatment of osteoarthritis and synovitis via intraarticular administration of their aminosugar compositions as in claims 1, 10 and 26, compositions in the form of particle, nanosphere, microsphere, pump, controlled release, subcutaneous injection or infusion, the treatment wherein the condition is not osteoarthritis and the combination therapy with antiinflammatory drugs and hexoaminidase inhibitors and the use of iminocyclitols as in claims 2, 4-6, 8-11, 16, 24, 25, 26, 29 and 30 and also the treatment of subchondral bone edema as in claims 1, 9 and 18. But Weidner's teaching indicates that synovitis can be treated via administration of aminosugars as instantly claimed via injection even though not specifically via intraarticular injection.

Petrus et al, drawn to arthritis, teach that during the inflammatory process vasoactive substances are released at the site of inflammation and cause edema (col. 1, line 36 through col. 2, line 8). Agents for treatment include glucosamine, its salts and N-acetylglucosamine (col. 5, lines 37-60; col. 6, line 14). Suitable routes of administration include subcutaneous, and intramuscular (col. 8, lines 15-17; col. 9, lines 35-36) using compositions in the form of suspensions and gels (col. 8, lines 19-21, 5, 7 and 29). In addition to aminosugars antiinflammatory agents can also be used (col. 8, lines 64-65 and col. 9, line 2). Petrus also

suggests delivery of the said compositions in the form of controlled release (col. 8, lines 26-30, limitation of claim 9) According to Petrus for patients who have difficulty in oral administration intramuscular and subcutaneous administration is an alternative (col. 9, lines 23-35, limitations of claim 10, 11 and 25). Even though Petrus does not specifically mention subchondral bone edema it is obvious from the teaching of Petrus that glucosamine, its salts and N-acetylglucosamine can be used in a method of treatment of subchondral bone edema via intraarticular or intramuscular administration using a composition in the form of a controlled release too.

Speck teaches a method of treating degenerative joint disease (joint cartilage degradation) by administration of N-acetyl glucosamine in combination with excipients via intraarticular, intramuscular, intravenous, or other injection or infusion methods (col. 1, lines 1-67; col. 5 line 15 through col. 6, line 34; limitations of claim 10-11 and 25). The teaching of Speck regarding the mode of administration of N-acetylglucosamine, especially intraarticular and infusion methods for the treatment of cartilage degradation means that the same modes of administration can also be used in the methods of treatment as instantly claimed.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a formulation comprising amino sugars and use it in a method of treatment as instantly claimed since the active agents and the methods of treatment via the different forms and modes of administration using them individually are seen to be taught/suggested in the prior art.

One of ordinary skill in the art would be motivated to make compositions comprising aminosugars including various forms of compositions and modes of administration and use them in a method of treatment of subchondral bone edema and synovitis as instantly claimed since

active agents like glucosamine, galactosamine are responsible for the synthesis of proteoglycans that are present in the synovial fluid (Weidner, page 2, line 20) and the said aminosugars are well known agents for the synthesis of proteoglycans and the said treatment as taught in the prior art above.

It is well within the purview of one of ordinary skill in the art to adjust ratios and substitute structurally similar active agents and make compositions in different forms since similarity in structure and function/utility entail motivation for use in the instant compositions and methods. One of skill in the art would also be motivated to look for other active agents and formulation that are more efficient and have enhanced beneficial effects.

Claims 3-8 and 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weidner (WO 03/002117, of record) in view of Speck (US 4,870,061, of record), Burger (US 5,843,919, of record), Woerly (US 5,863,551, of record) and Nanba et al (US 5,169,636, of record).

The teachings of Weidner, Speck and Burger are as above. However, they do not teach a method of treatment that uses the formulation as instantly claimed in the form of a hydrogel, matrix and a combination therapy which includes antiinflammatory drugs and hexoaminidase inhibitors.

Burger, drawn to arthritis/osteoarthritis, teaches the treatment of these conditions using compositions comprising a combination of glucosamine and N-acetyl glucosamine (col. 1, lines 14-45; col. 2, lines 19-44). The said compositions are preferably in the form of solutions, suspensions, gels, systemic implant or an injection or injection into an affected joint (col. 3, lines

20-56). According to Burger medications for treatment of osteoarthritis (which involves cartilage degradation) include antiinflammatory compounds (col. 1, lines 32-35, limitation of claim 30). This means that antiinflammatory drugs can be combined with aminosugars for the treatment of cartilage degradation since both are useful for the same purpose. Even though Burger does not specifically exemplify the said method of treatment wherein the composition is injected intraarticularly his teaching regarding the injection into the affected joint suggests that compositions comprising glucosamine and N-acetylglucosamine including galactosamine and its N-acetyl derivative and antiinflammatory drugs can be directly administered into the affected joints (intraarticular injection).

Woerly teaches polymer hydrogels as implants for treating tissue replacement and regeneration (col. 1, lines 5-18, limitations of claims 4 and 7). Another aspect of his invention is the use of a polymer matrix (col. 5, lines 33-40 and lines 52-56, limitation of claims 3 and 8). The polymer matrices can include aminosugars like glucosamine, N-acetyl glucosamine, galactosamine and N-acetylgalactosamine (col. 8, lines 31-34). Even though Woerly does not exemplify the use of such matrices and gels in a method for the treatment of the conditions as instantly claimed one of skill in the art will recognize that such matrices containing the monomeric aminosugars can be made and used in the instant methods of treatment.

Nanba et al, drawn to liposomes, teach compositions comprising oligosaccharides comprising glucosamine and galactosamine residues entrapped by liposomes (col. 1, lines 60 col. 2, line 68; limitation of claim 5). The liposomes containing the aminosugars are made into particles having a diameter of about 0.03-0.8 microns (microspheres, col. 5, lines 43-46, limitations of claims 4-5 and 8-for matrix). According to Nanba liposomes are models for

biological membranes and are effective in stabilizing drugs and achieving sustained release of drugs in vivo. The duration of the efficacy of drugs can be prolonged (col. 1, lines 25-28; lines 37-39). Even though Nanba teaches oligosaccharides comprising glucosamine and galactosamine residues, one of skill in the art will recognize that the monomeric aminosugars can also be used to make the same liposomal formulations as instantly claimed and used in the instant methods of treatment. Nanba teaches only a matrix comprising his aminosugars in the form of liposomal particles and microspheres. Even though he does not teach the use of his compositions for treating synovitis, subchondral bone edema and cartilage degradation one of ordinary skill in the art will recognize that his compositions can be used for that purpose in view of the teachings of Weidner and Speck.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a formulation comprising amino sugars and use it in a method of treatment as instantly claimed since the active agents and the methods of treatment via the use of forms like gels, implants, matrix and modes of administration using them individually are seen to be suggested in the prior art.

One of ordinary skill in the art would be motivated to make compositions comprising aminosugars including various forms of compositions like matrix, gels and implants and modes of administration and use them in a method of treatment as instantly claimed since active agents like glucosamine and galactosamine are responsible for the synthesis of proteoglycans which are present in synovial joint fluid and the said aminosugars are well known agents for such repair and said treatment as taught in the prior art above. Also, gels and implants have the advantage of delivering the active agents directly to site where they are needed.

It is well within the purview of one of ordinary skill in the art to adjust ratios and substitute structurally similar active agents and make compositions in different forms since similarity in structure and function/utility entail motivation for use in the instant compositions and methods. One of skill in the art would also be motivated to look for other active agents and formulation that are more efficient and have enhanced beneficial effects.

Response to Applicants Remarks

In response to applicants' arguments the rejections above are made of record necessitated by amendment. Applicants have provided the following arguments:

1. Weidner teaches the aminosugars have provided some relief of symptoms. According to him a combination of niacinamide and aminosugar complex is needed. One of ordinary skill in the art would not use aminosugar alone.

2. Speck teaches that injection of glucosamine is undesirable because an injection preparation is unstable and has to be prepared and stored in an acidic pH value and neutralized before use. A local anesthetic such as lidocaine is necessary, which can cause side effects. Recitation of all possible ways to introduce glucosamine does not amount to an obvious method of achieving successful result.

3. Nanba does not disclose or suggest treating synovitis or subchondral bone edema.

4. Burger teaches that little if any success has been reported in the treatment of osteoarthritis with glucosamine and omega-3 fatty acids. Therefore one of skill in the art would not use an aminosugar alone as claimed.

5. The N-acetylglucosamine in Woerly's matrix is a component of the structure and not the targeted element. There is no reference to the method of treatment as instantly claimed.

6. The Examiner fails to cite where Wong possessed the concept of using iminocyclitols in combination with glucosamine and galactosamine and their salts. This may seem obvious to the examiner but Wong does not teach this combination.

7. Petrus discloses that aminosugar alone is not effective but zinc acetate along with glucosamine sulfate was needed to treat osteoarthritis. Therefore one of ordinary skill in the art would not use a therapeutically effective amount of an aminosugar via intraarticular injection as presently claimed.

Applicants' arguments have been considered but are not found to be persuasive.

1. The fact that aminosugars have provided some relief means that they can be used in the claimed method of treatment. This is borne out in the teachings of the prior art. Otherwise all the prior art cited above would not disclose the use of the aminosugars for the same purpose. In all of them the aminosugars as instantly claimed are used. Weidner may have used a complex of an aminosugar with niacinamide. This does not mean that the aminosugar cannot be used alone. There is also no teaching in Weidner that it should not be used alone.

2. Speck teaches the undesirability of using glucosamine sulfate. This is not true of glucosamine, galactosamine and its derivatives and salts as instantly claimed.

3. Nanba's teaching is with regard to making liposomes using aminosugars. The liposomes taught by him can be used by one of ordinary skill in the art for making liposomes of the instant aminosugars and use them in the instant methods of treatment. Nanba does not have to specifically teach the use of liposomes in treating synovitis and subchondral bone edema.

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. “The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art.” *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000).

4. Burger’s teaching also does not mean that aminosugars should not be used alone at all. As long as the art reports some success aminosugars can and will be used for the claimed methods of treatment since such use is suggested by the art.

5. The N-acetylglucosamine in Woerly’s matrix may be a component of the structure. Since aminosugars are known for the claimed methods of treatment as taught by Weidner (synovitis) and Petrus (edema), if the aminosugar(s) is/are present in the matrix and if the matrix is administered to the patient having the recited conditions it will have a beneficial effect on the said condition.

6. At the pages and lines cited by the Applicants in Petrus there is no specific teaching that aminosugar alone is not effective. At the cited column and lines Petrus just discloses that zinc acetate and aminosugar was used in his method. This does not mean that the aminosugar cannot be used alone, especially when the other citations teach that they can be used alone.

Conclusion

Claims 1-11, 16-18 and 23-30 are rejected

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ganapathy Krishnan/
Examiner, Art Unit 1623

/Shaojia Anna Jiang/
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